Claims

1. An adjuvant comprising an isolated conjugate of a CD28 and/or CD40 antibody and at least one antigen wherein said conjugate consists of an oligomeric complex wherein the antibody valency of the complex does not exceed an average of about five antibody molecules per complex.

2. An adjuvant according to Claim 1 wherein said conjugate consists an average of one to four antibody molecules per complex.

3. An adjuvant according to Claim 2 wherein said complex consists an average of one to three antibody molecules per complex.

4. An adjuvant according to Claim 2 or 3 wherein said complex consists of one to two antibody molecules per complex.

5. A vaccine composition comprising a conjugate according to any of Claims 1-4.

6. A vaccine according to Claim 5 wherein said composition further comprises a carrier.

7. A vaccine according to Claim 5 or 6 wherein said composition further comprises a second adjuvant.

8. An vaccine according to Claim 7 wherein said composition comprises a mixture of a CD40 adjuvant and a CD28 adjuvant according to any of Claims 1-4.

9. An adjuvant according to any of Claims 1-4 wherein said antigen is a T-cell dependent antigen.

10. An adjuvant according to any of Claims 1-4 wherein said antigen is a T- cell independent antigen.

11. An adjuvant according to Claim 9 or 10 wherein said antigen is derived from a pathogenic bacterium.

12. An adjuvant according to Claim 11 wherein said antigen is derived from a bacterial species selected from the group consisting of: *Staphylococcus aureus; Staphylococcus epidermidis; Enterococcus faecalis; Mycobacterium tuberculsis; Streptococcus group B; Streptoccocus pneumoniae; Helicobacter pylori; Neisseria gonorrhea; Streptococcus group A; Borrelia burgdorferi; Coccidiodes immitis; Histoplasma sapsulatum; Neisseria meningitidis ; Shigella flexneri; Escherichia coli; Haemophilus influenzae.*

13. An adjuvant according to Claim 9 or 10 wherein said antigen is derived from a viral pathogen.

14. An adjuvant according to Claim 13 wherein said antigen is derived from a viral pathogen selected from the group consisting of: Human Immunodeficiency Virus (HIV1 & 2); Human T Cell Leukaemia Virus (HTLV 1 & 2); Ebola virus; human papilloma virus (e.g. HPV-2, HPV-5, HPV-8 HPV-16, HPV-18, HPV-31, HPV-33, HPV-52, HPV-54 and HPV-56); papovavirus; rhinovirus; poliovirus; herpesvirus; adenovirus; Epstein Barr virus; influenza virus, hepatitis B and C viruses.

15. An adjuvant according to Claim 9 or 10 wherein said antigen is derived from a parasitic pathogen.

16. An adjuvant according to Claim 15 wherein said antigen is derived a parasistic pathogen selected from the group consisting of: *Trypanosoma spp, Schistosoma spp* or *Plasmodium spp.*

17. An adjuvant according to Claim 9 or 10 wherein said antigen is derived from a fungal pathogen.

18. An adjuvant according to Claim 17 wherein said antigen is derived from a fungal pathogen which is of the genus *Candida spp.*

19. An adjuvant according to Claim 9 or 10 wherein said antigen is a tumour specific antigen or a tumour associated antigen.

20. An adjuvant according to Claim 19 wherein said antigen is a ganglioside antigen.

21. An adjuvant according to Claim 19 or 20 wherein said antigen is MUC-1.

22. An adjuvant according to Claim 9 or 10 wherein said antigen is a hormone or hormone receptor.

23. An adjuvant according to Claim 22 wherein said antigen is the N-methyl-D aspartate receptor, or part thereof.

24. An adjuvant according to Claim 9 or 10 wherein said antigen is a prion protein.

25. An adjuvant according to Claim 24 wherein said antigen is an amyloid protein.

26. An adjuvant according to Claim 25 wherein wherein said antigen is amyloid β or part thereof.

27. An adjuvant according to Claim 9 or 10 wherein said antigen is a sperm antigen.

28. An adjuvant according to Claim 9 or 10 wherein said antigen is an addictive drug.

29. An adjuvant according to Claim 28 wherein said drug is selected from the group consisting of: cocaine; nicotine; or heroin.

30. A method to immunise an animal to an antigen, comprising administering an effective amount of a conjugate according to any of Claims 1-29 sufficient to stimulate an immune response to said antigen.

31. A method according to Claim 30 wherein said animal is human.

32. A method according to Claim 30 wherein said animal is selected from the group consisting of: mouse; rat; hamster; goat; cow, horse, pig, dog, cat or sheep.

33. A method according to any of Claims 30-32 wherein said route of administration is intradermal, subcutaneous, intramuscular or intranasal.

34. A method according to Claim 33 wherein said route is intranasal.

35 An antibody obtainable by the method according to any of Claims 30-34.

36. An antibody according to Claim 35 wherein said antibody is a monoclonal antibody or binding fragment thereof.

37. An antibody according to Claim 36 wherein said antibody is a humanised antibody.

38. An antibody according to Claim 36 wherein said antibody is a chimeric antibody.

39. An antibody according to any of Claims 36-38 wherein said antibody is an opsonic antibody.

40. A method for preparing a hybridoma cell-line producing monoclonal antibodies according to Claim 36 comprising the steps of:

i) immunising an immunocompetent mammal with a conjugate or, composition according 1-29;

ii) fusing lymphocytes of the immunised immunocompetent mammal with myeloma cells to form hybridoma cells;

iii) screening monoclonal antibodies produced by the hybridoma cells of step (ii) for binding activity to the antigen of the conjugate;

iv) culturing the hybridoma cells to proliferate and/or to secrete said monoclonal antibody; and

v) recovering the monoclonal antibody from the culture supernatant.

41. A hybridoma cell-line obtainable by the method according to Claim 40.

42. A method to crosslink an antibody, wherein said antibody is capable of binding a CD28 or CD40 receptor polypeptide, and at least one antigen characterised in that reaction conditions are provided which select for conjugates with low antibody valency.

43. A method to prepare an adjuvant according to any of Claims 1-4 or 9-29 comprising fractionation of a conjugation reaction mixture.

44. A method according to Claim 43 said fractionation comprises the following steps:

i) providing a reaction mixture consisting of a heterogeneous crosslinked antibody: antigen conjugate complex;

ii) separating the reaction mixture into fractions containing conjugates of defined size; and optionally

iii) isolating conjugates with a desired antibody valency.

45. A method according to Claim 44 wherein said fraction contains a conjugate complex with an antibody valency of about on average five antibody molecules per complex.

46. A method according to Claim 44 wherein said fraction contains a complex with an antibody valency of between one to four antibodies per complex.

47. A method according to Claim 44 whereinsaid fraction contains a complex with an antibody valency of between one and three antibodies per complex.

48. A method according to Claim 44 wherein said fraction contains a complex of two antibody molecules.

49. A method according to Claim 44 wherein said conjugate is a single antibody linked to at least one antigen.

50. A conjugate obtainable by the fractionation method according to any of Claims 43-49.